

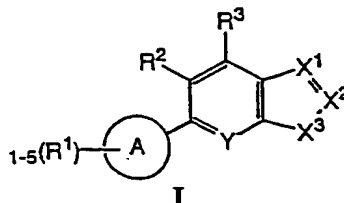
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

What is claimed is:

1. (original) A compound for inhibiting ALK according to formula I,



or a pharmaceutically acceptable salt, stereoisomer, prodrug or metabolite thereof, wherein,

A is a five- to ten-membered ring containing up to three heteroatoms; provided A is not a saturated alicyclic when X^2 is =N-, X^3 is -O-, and A is a pyridin-4-yl;

each of R^1 , R^2 and R^3 is independently selected from -H, halo, trihalomethyl, -CN, -NO₂, -OR⁴, -N(R⁴)R⁴, -S(O)₀₋₂R⁴, -SO₂N(R⁴)R⁴, -CO₂R⁴, -C(=O)N(R⁴)R⁴, -C(=O)R⁴, -C(=NR⁵)N(R⁴)R⁴, -C(=NR⁵)R⁴, -N(R⁴)SO₂R⁴, -N(R⁴)C(O)R⁴, -NCO₂R⁴, optionally substituted alkoxy, optionally substituted C₁₋₆ alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆ alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆ alkyl;

two adjacent of R^1 , together with the annular atoms to which they are attached, can form a five- to six-membered ring containing up to two heteroatoms and optionally substituted with up to four of R¹⁰;

R^2 and R^3 , together with the annular atoms to which they are attached, can form a five- to six-membered ring containing up to two heteroatoms and optionally substituted with up to five of R⁶;

each R⁴ is selected from -H, optionally substituted C₁₋₆ alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆ alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆ alkyl;

two of R⁴, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl, said optionally substituted five- to seven-membered heterocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R⁵ is selected from -H, -CN, -NO₂, -OR⁴, -S(O)₀₋₂R⁴, -CO₂R⁴, optionally substituted C₁₋₆ alkyl, optionally substituted C₂₋₆ alkenyl, and optionally substituted C₂₋₆ alkynyl;

Y is =N- or =C(R⁹)-;

X¹ and X² are each independently either =N- or =C(R⁹)-;

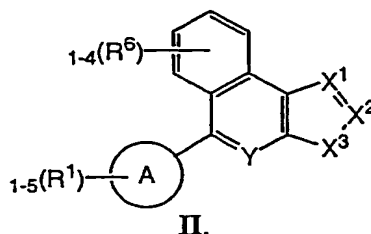
X³ is selected from -N(R⁷)-, -O-, and -S-;

R⁷ is selected from -H, optionally substituted C₁₋₆alkyl, -SO₂N(R⁴)R⁴, -CO₂R⁴, -C(=O)N(R⁴)R⁴, -C(=NR⁵)N(R⁴)R⁴, -C(=NR⁵)R⁴, -C(=O)R⁴, optionally substituted alkoxy, optionally substituted aryl, optionally substituted aryl C₁₋₆ alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆ alkyl;

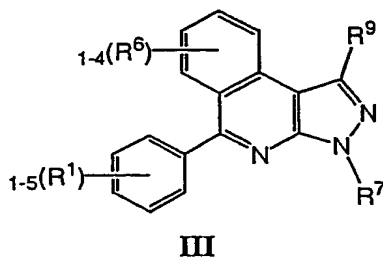
each of R⁶, R⁸, R⁹ and R¹⁰ is independently selected from -H, halo, trihalomethyl, -CN, -NO₂, -OR⁴, -N(R⁴)R⁴, -S(O)₀₋₂R⁴, -SO₂N(R⁴)R⁴, -CO₂R⁴, -C(=O)N(R⁴)R⁴, -C(=NR⁵)N(R⁴)R⁴, -C(=NR⁵)R⁴, -N(R⁴)SO₂R⁴, -N(R⁴)C(O)R⁴, -NCO₂R⁴, -C(=O)R⁴, optionally substituted alkoxy, optionally substituted C₁₋₆ alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆ alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆ alkyl; provided when R⁹ is aryl, heteroaryl, -C(H)=C(H)R or -C(H)=NR, where R is an optionally substituted alkyl, cycloalkyl, heteroalicyclic, aryl, or heteroaryl, then Y is not =C(H)-; and

two adjacent of R⁶, together with the annular atoms to which they are attached, can form an optionally substituted five- to seven-membered ring containing up to two heteroatoms.

2. (original) The compound according to claim 1, wherein R² and R³, together with the carbons to which they are attached, form a five- to six-membered ring containing up to two heteroatoms and optionally substituted with up to four of R⁶.
3. (original) The compound according to claim 2, wherein said five- to six-membered ring is an aryl or a heteroaryl.
4. (original) The compound according to claim 3, wherein said five- to six-membered ring is phenyl or pyridyl.
5. (original) The compound according to claim 4, of formula II,



6. (original) The compound according to claim 5, wherein X^1 is $=C(R^9)-$, X^2 is $=N-$, and X^3 is $=N(R^7)-$.
7. (original) The compound according to claim 6, wherein Y is $=N-$.
8. (original) The compound according to claim 7, wherein A is either a five- to ten-membered aryl or a five- to ten-membered heteroaryl containing up to three heteroatoms.
9. (original) The compound according to claim 8, wherein A is either a five- or six-membered aryl or a five- or six-membered heteroaryl containing up to three heteroatoms.
10. (original) The compound according to claim 9, wherein R^1 is selected from -H, halo, trihalomethyl, -CN, $-OR^4$, $-N(R^4)R^4$, $-SO_2N(R^4)R^4$, $-CO_2R^4$, $-C(=O)N(R^4)R^4$, $-C(=NR^5)N(R^4)R^4$, $-C(=NR^5)R^4$, $-N(R^4)SO_2R^4$, $-N(R^4)C(O)R^4$, $-NCO_2R^4$, optionally substituted alkoxy, optionally substituted C_{1-6} alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C_{1-6} alkyl.
11. (original) The compound according to claim 10, of formula III,



wherein at least one of R^1 is -OH.

12. (original) The compound according to claim 11, wherein the compound is either a 3-(3H-pyrazolo[3,4-c]isoquinolin-5-yl)-phenol or a 4-(3H-pyrazolo[3,4-c]isoquinolin-5-yl)-phenol.
13. (original) The compound according to claim 12, wherein R^9 is selected from -H, trihalomethyl, optionally substituted alkoxy, optionally substituted C_{1-6} alkyl, optionally substituted aryl C_{1-6} alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C_{1-6} alkyl.
14. (original) The compound according to claim 13, wherein R^6 is selected from -H, halo, trihalomethyl, -CN, $-OR^4$, $-N(R^4)R^4$, $-CO_2R^4$, $-C(=O)N(R^4)R^4$, $-N(R^4)SO_2R^4$,

-N(R⁴)C(O)R⁴, -NCO₂R⁴, -C(=O)R⁴, optionally substituted C₁₋₆ alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl C₁₋₆ alkyl, and a six- or seven-membered heteroalicyclic formed by two adjacent of R⁶, together with the annular atoms to which they are attached, said six- or seven-membered heteroalicyclic containing up to two heteroatoms.

15. (original) The compound according to claim 14, wherein R⁶ is selected from -H, halo, -OR⁴, -N(R⁴)R⁴, optionally substituted C₁₋₆ alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl C₁₋₆ alkyl, and a six- or seven-membered heteroalicyclic formed by two adjacent of R⁶, together with the annular atoms to which they are attached, said six- or seven-membered heteroalicyclic containing up to two heteroatoms.
16. (original) The compound according to claim 15, wherein at least one of R⁶ is optionally substituted C₁₋₆ alkoxy.
17. (original) The compound according to claim 16, wherein at least one of R¹ is halogen or methyl.
18. (original) The compound according to claim 17, wherein R⁹ is selected from -H, trihalomethyl, and optionally substituted C₁₋₆ alkyl.
19. (original) The compound according to claim 15, wherein at least one of R⁶ is C₁₋₆ alkoxy substituted with a heteroalicyclic.
20. (original) The compound according to claim 19, wherein said heteroalicyclic is selected from the group consisting of dioxolanyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, pyrrolidinyl, morpholinyl, quinuclidinyl, tetrahydrofuryl, tetrahydropyranyl, thiamorpholinyl, thiamorpholinyl sulfoxide, 2,5-diaza-bicyclo[2.2.1]heptanyl, and thiamorpholinyl sulfone.
21. (original) The compound according to claim 15, wherein at least one of R⁶ is C₁₋₆ alkoxy substituted with at least one additional of an optionally substituted alkoxy, an amino, an optionally substituted dialkylamino, and an optionally substituted monoalkylamino.

22. (original) The compound according to claim 1, selected from Table 3.

Table 3

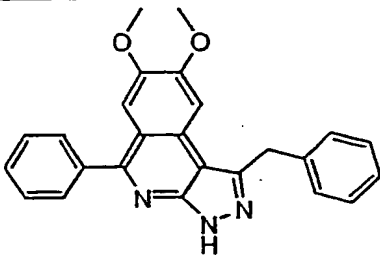
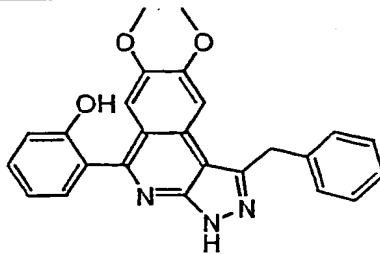
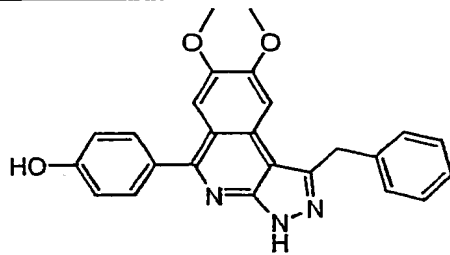
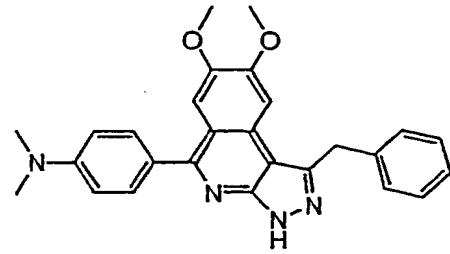
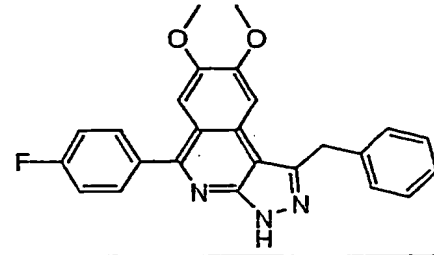
Entry	Name	Structure
1	7,8-bis(methoxy)-5-phenyl-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinoline	
2	2-[7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
3	4-[7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
4	4-[7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-N,N-dimethylaniline	
5	5-(4-fluorophenyl)-7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinoline	

Table 3

Entry	Name	Structure
6	5-(4-nitrophenyl)-7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinoline	
7	4-[3-methyl-7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
8	3-[7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
9	4-[7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzene-1,2-diol	
10	4-{7,8-bis(methoxy)-1-[(4-methylphenyl)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	

Table 3

Entry	Name	Structure
11	5-(1,3-benzodioxol-5-yl)-7,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinoline	
12	4-(7,8-bis(methoxy)-1-([4-(methoxy)phenyl]methyl))-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
13	4-{7,8-bis(methoxy)-1-[(2-methylphenyl)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
14	4-{7,8-bis(methoxy)-1-[(3-methylphenyl)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
15	4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
16	2-[7,8-bis(methyloxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-6-fluorophenol	
17	3-[7,8-bis(methyloxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-4-nitrophenol	
18	4-[7,8-bis(methyloxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzoic acid	
19	4-[7,8-bis(methyloxy)-1-(1-phenylethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
20	4-[1-{{[3,4-bis(methyloxy)phenyl]methyl}-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl}]phenol	

Table 3

Entry	Name	Structure
21	4-(7,8-bis(methoxy)-1-([3-(methoxy)phenyl]methyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
22	4-[1-ethyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
23	7,8-bis(methoxy)-1-(phenylmethyl)-5-pyridin-4-yl-3H-pyrazolo[3,4-c]isoquinoline	
24	4-[6,7,8-tris(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
25	4-[1-methyl-6,7,8-tris(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
26	4-[8-(methyloxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
27	4-[7,8-bis(methyloxy)-1-(trifluoromethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
28	4-[1-(1-methylethyl)-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
29	4-[7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
30	4-[7-methyl-8-(methyloxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
31	4-[1-methyl-6,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
32	4-[6,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
33	4-[6,8-bis(methoxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
34	4-[6,7,8-tris(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
35	4-[1-methyl-7,8,9-tris(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
36	4-[1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
37	2-methyl-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
38	4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-(methyloxy)phenol	
39	4-{1-methyl-8-(methyloxy)-7-[(2-morpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
40	2-(ethyloxy)-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
41	2-chloro-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
42	2-fluoro-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
43	4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-nitrophenol	
44	2-bromo-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
45	1-([5-(4-hydroxyphenyl)-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-1-yl)methyl)pyrrolidin-2-one	

Table 3

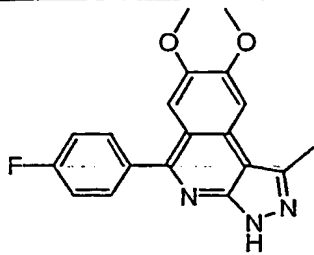
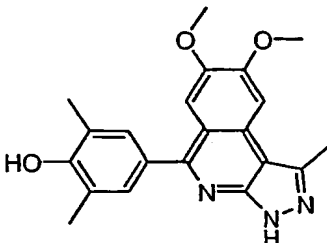
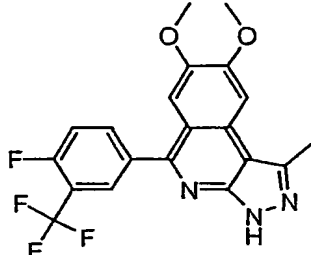
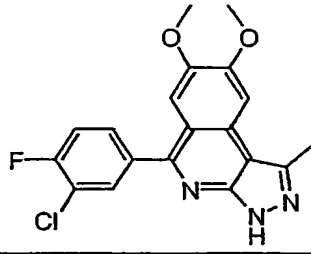
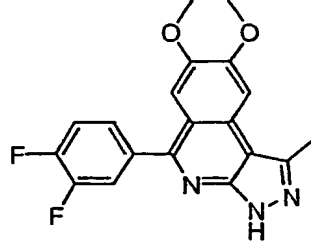
Entry	Name	Structure
46	5-(4-fluorophenyl)-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	
47	2,6-dimethyl-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
48	5-[4-fluoro-3-(trifluoromethyl)phenyl]-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	
49	5-(3-chloro-4-fluorophenyl)-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	
50	5-(3,4-difluorophenyl)-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	

Table 3

Entry	Name	Structure
51	1-methyl-7,8-bis(methoxy)-5-[3-(trifluoromethyl)phenyl]-3H-pyrazolo[3,4-c]isoquinoline	
52	5-(4-fluoro-3-methylphenyl)-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	
53	5-(3-bromo-4-fluorophenyl)-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	
54	4-{1-methyl-7-(methoxy)-8-[(piperidin-4-ylmethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
55	4-{1-methyl-8-(methoxy)-7-[(piperidin-4-ylmethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	

Table 3

Entry	Name	Structure
56	1-methyl-7,8-bis(methyloxy)-5-(3-methylphenyl)-3H-pyrazolo[3,4-c]isoquinoline	
57	5-(3-bromophenyl)-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinoline	
58	4-[8-(ethyloxy)-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
59	4-[1-methyl-8,9-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
60	4-[7-(ethyloxy)-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
61	4-{1-methyl-8-(methyloxy)-9-[(piperidin-4-ylmethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
62	4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-(1-methylethyl)phenol	
63	2-ethyl-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
64	4-(1-methyl-8-(methyloxy)-9-[[1-(1-methylpiperidin-4-yl)methyl]oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
65	4-(1-methyl-7-(methyloxy)-8-[[1-(1-methylpiperidin-4-yl)methyl]oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
66	4-[1,7-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
67	1,1-dimethylethyl 4-[5-(4-hydroxyphenyl)-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-1-yl]piperidine-1-carboxylate	
68	4-[7,8-bis(methoxy)-1-piperidin-4-yl-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
69	2-chloro-4-[1-methyl-8,9-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
70	2-fluoro-4-[1-methyl-8,9-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
71	2-methyl-4-[1-methyl-8,9-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
72	2-bromo-4-[1-methyl-8,9-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
73	4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzonitrile	
74	N'-hydroxy-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzenecarboximidamide	
75	5-hydroxy-2-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-4H-pyran-4-one	
76	2-[(difluoromethyl)oxy]-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
77	5-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]pyridin-2-ol	

Table 3

Entry	Name	Structure
78	4-[1,9-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
79	4-[6,9-difluoro-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
80	2-bromo-4-{1-methyl-8-(methyloxy)-9-[(2-morpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
81	2-chloro-4-{1-methyl-8-(methyloxy)-9-[(2-morpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
82	4-(7,8-bis(methyloxy)-1-[[[(phenylmethyl)amino]methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
83	2,5-dimethyl-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
84	2,3-dichloro-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
85	2,5-dichloro-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
86	2,3-dimethyl-4-[1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
87	2-bromo-4-(1-methyl-8-(methoxy)-9-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
88	2-chloro-4-(1-methyl-7-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
89	4-[9-fluoro-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
90	4-(1-methyl-8-(methyloxy)-9-[[2-(methyloxy)ethyl]oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
91	2-chloro-4-(1-methyl-8-(methyloxy)-9-[[1-(methylpiperidin-4-yl)methyl]oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
92	4-[6-bromo-1,7-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
93	4-[6-fluoro-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
94	4-[9-chloro-1,7-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
95	2-chloro-4-[8-{{[(1-ethylpiperidin-4-yl)methyl]oxy}-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl}]phenol	
96	3-chloro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
97	4-(1-methyl-8,9-bis{{[2-(methyloxy)ethyl]oxy}}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
98	4-(1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
99	2-chloro-4-(1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
100	2-bromo-4-(1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
101	2-chloro-4-[1,7-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
102	2-bromo-4-[1,7-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
103	2-chloro-4-[1-methyl-8-([1-(1-methylethyl)piperidin-4-yl)methoxy]-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
104	4-[9-bromo-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
105	4-[7-chloro-9-fluoro-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
106	4-[8-{{[(1-acetylpiperidin-4-yl)methyl]oxy}-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
107	4-[9-{{[(1-acetylpiperidin-4-yl)methyl]oxy}-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-bromophenol	
108	2-chloro-4-(1-methyl-9-(methyloxy)-8-{{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl})phenol	
109	4-[7-fluoro-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
110	2-chloro-4-(1-methyl-8,9-bis{{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl})phenol	

Table 3

Entry	Name	Structure
111	2-bromo-4-(1-methyl-8,9-bis{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
112	2-chloro-4-(1-methyl-8-(methyloxy)-9-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
113	2-bromo-4-(1-methyl-8-(methyloxy)-9-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
114	3-fluoro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
115	2-chloro-4-(1-methyl-7-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
116	2-bromo-4-(1-methyl-7-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
117	2-chloro-4-(1-methyl-7,8-bis{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
118	2-bromo-4-(1-methyl-7,8-bis{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
119	1-methyl-7,8-bis(methyloxy)-5-(1H-pyrazol-5-yl)-3H-pyrazolo[3,4-c]isoquinoline	
120	4-(6,9-difluoro-1-methyl-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
121	2-chloro-5-fluoro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
122	2-bromo-5-fluoro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
123	4-[9-fluoro-1-methyl-7,8-bis(methyloxy)-3H-benzo[e]indazol-5-yl]phenol	
124	2-hydroxy-5-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzoic acid	
125	3-fluoro-4-(1-methyl-7-(methyloxy)-8-[[2-(methyloxy)ethyl]oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
126	4-(6,9-difluoro-1-methyl-8-{{2-(methyloxy)ethyl}oxy})-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-3-fluorophenol	
127	2-chloro-4-(6,9-difluoro-1-methyl-8-{{2-(methyloxy)ethyl}oxy})-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
128	2-chloro-4-[8-(ethyloxy)-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
129	2-chloro-4-[6-chloro-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
130	3-fluoro-4-(1-methyl-9-(methyloxy)-8-{{2-(methyloxy)ethyl}oxy})-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
131	2-chloro-4-(1,7-dimethyl-8-([2-(methyloxy)ethyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
132	3-fluoro-4-(6-fluoro-1-methyl-7-(methyloxy)-8-([2-(methyloxy)ethyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
133	2-chloro-4-[1-methyl-8-[(1-methylethyl)oxy]-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
134	2-chloro-4-{1-methyl-7-(methyloxy)-8-[(2-methylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
135	2-bromo-5-fluoro-4-(1-methyl-7-(methyloxy)-8-([2-(methyloxy)ethyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
136	4-[7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
137	4-[7,8-bis(methoxy)-1-(trifluoromethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
138	4-[7,8-bis(methoxy)-1-[(methoxy)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
139	2-chloro-4-(1-methyl-3H-[1,3]dioxolo[4,5-g]pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
140	2-chloro-4-(1-methyl-8,9-dihydro-3H-[1,4]dioxino[2,3-g]pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
141	2-chloro-4-(1-methyl-9,10-dihydro-3H,8H-[1,4]dioxepino[2,3-g]pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
142	2-chloro-4-[7-[(difluoromethyl)oxy]-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
143	2-chloro-5-fluoro-4-(6-fluoro-1-methyl-9-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
144	2-chloro-4-(6,9-difluoro-1-methyl-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-5-fluorophenol	
145	2-chloro-4-(11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenol	
146	2-chloro-5-fluoro-4-(11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenol	

Table 3

Entry	Name	Structure
147	2-chloro-4-[1-methyl-6,7,8-tris(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
148	2-bromo-4-(6,9-difluoro-1-methyl-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-5-fluorophenol	
149	7-(3-chlorophenyl)-11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinoline	
150	2-chloro-5-fluoro-4-(6-fluoro-1-methyl-8,9-dihydro-3H-[1,4]dioxino[2,3-g]pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
151	2-chloro-4-{1-methyl-7-(methyloxy)-8-[(tetrahydrofuran-2-ylmethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
152	2-chloro-4-{1-methyl-7-(methyloxy)-8-[(tetrahydro-2H-pyran-2-ylmethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	

Table 3

Entry	Name	Structure
153	2-chloro-4-{1-methyl-7-(methoxy)-8-[(2,2,2-trifluoroethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
154	2-chloro-5-fluoro-4-[9-fluoro-1-methyl-6,7,8-tris(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
155	5-(3-chloro-4-hydroxyphenyl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
156	6,9-difluoro-5-(2-fluorophenyl)-1-methyl-8-[[2-(methoxy)ethyl]oxy]-3H-pyrazolo[3,4-c]isoquinoline	
157	2-chloro-4-{8-[(difluoromethyl)oxy]-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
158	2-chloro-4-(6,11-difluoro-1-methyl-8,9-dihydro-3H-[1,4]dioxino[2,3-g]pyrazolo[3,4-c]isoquinolin-5-yl)-5-fluorophenol	

Table 3

Entry	Name	Structure
159	4-(1-methyl-3H-benzo[e]indazol-5-yl)phenol	
160	6-fluoro-7-(2-fluorophenyl)-11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinoline	
161	2-chloro-4-{1-methyl-7-(methyloxy)-8-[(tetrahydro-2H-pyran-4-ylmethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
162	2-chloro-4-[8-{[2-(ethyloxy)ethyl]oxy}-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
163	N-[4-(6-fluoro-11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenyl]acetamide	
164	3-fluoro-4-(6-fluoro-11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenol	

Table 3

Entry	Name	Structure
165	2-chloro-5-fluoro-4-(6-fluoro-11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenol	
166	2-chloro-4-[8-(cyclopentyloxy)-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
167	2-chloro-4-(1-methyl-7-(1-methylethyl)-8-{{[2-(methyloxy)ethyl]oxy}}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
168	2-chloro-4-[9-ethyl-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
169	2-chloro-4-(6,9-difluoro-1-methyl-8-{{[(1-methylpiperidin-4-yl)methyl]oxy}}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
170	5-(3-chloro-4-hydroxyphenyl)-8-fluoro-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-6-ol	

Table 3

Entry	Name	Structure
171	2-chloro-4-(6-fluoro-1-methyl-7-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
172	2-chloro-4-(6-fluoro-1-methyl-8,9-bis{[2-(methoxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
173	5-[3-chloro-4-(methoxy)phenyl]-6-fluoro-1-methyl-7-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinoline	
174	5-[3-chloro-4-(methoxy)phenyl]-8-fluoro-1-methyl-7-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-6-ol	
175	5-[3-chloro-4-(methoxy)phenyl]-1-methyl-7,8-bis(methoxy)-3H-pyrazolo[3,4-c]isoquinoline	

Table 3

Entry	Name	Structure
176	2-chloro-4-{6-fluoro-1-methyl-7-(methyloxy)-8-[(2-piperidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
177	2-chloro-4-[8-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-6-fluoro-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
178	2-chloro-4-[8-{[2-(diethylamino)ethyl]oxy}-6-fluoro-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
179	2-chloro-4-(6-fluoro-1-methyl-7-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
180	6,9-difluoro-5-furan-3-yl-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
181	6,9-difluoro-5-furan-2-yl-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

Table 3

Entry	Name	Structure
182	2-chloro-4-(6-fluoro-1-methyl-9-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
183	2-bromo-4-(6-fluoro-1-methyl-9-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
184	2-chloro-5-fluoro-4-(6-fluoro-1-methyl-9-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
185	4-(6-fluoro-1-methyl-9-(methoxy)-8-[[1-methylpiperidin-4-yl)methyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-2-methylphenol	
186	2-chloro-4-(6,9-difluoro-1-methyl-8-[(2-piperidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
187	2-chloro-4-(8-[[2-(4-ethylpiperazin-1-yl)ethyl]oxy]-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
188	2-chloro-4-(8-{[2-(diethylamino)ethyl]oxy}-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
189	4-(6,9-difluoro-8-hydroxy-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-N-hydroxybenzenecarboximidamide	
190	3-(6,9-difluoro-8-hydroxy-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-N-hydroxybenzenecarboximidamide	
191	6,9-difluoro-5-(1H-indol-5-yl)-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
192	5-(1H-benzimidazol-6-yl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
193	5-(4-aminophenyl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

Table 3

Entry	Name	Structure
194	2-chloro-4-(6-fluoro-1-methyl-7-(methoxy)-8-{[2-(4-methylpiperazin-1-yl)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
195	5-(2-amino-1,3-thiazol-5-yl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
196	2-chloro-4-[8-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
197	2-chloro-4-(6-fluoro-1-methyl-9-(methoxy)-8-{[2-(4-methylpiperazin-1-yl)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
198	5-(6-aminopyridin-3-yl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
199	5-(5-amino-2-thienyl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

Table 3

Entry	Name	Structure
200	2-chloro-4-[8-{{3-(4-ethylpiperazin-1-yl)propyl}oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
201	2-chloro-4-(6-fluoro-1-methyl-9-(methyloxy)-8-{{3-(4-methylpiperazin-1-yl)propyl}oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
202	6,9-difluoro-5-(1H-indol-6-yl)-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
203	N-[5-(6,9-difluoro-8-hydroxy-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)-1,3-thiazol-2-yl]acetamide	
204	5-(3-chlorophenyl)-8-{{2-(4-ethylpiperazin-1-yl)ethyl}oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinoline	
205	5-(3-aminophenyl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

Table 3

Entry	Name	Structure
206	2-chloro-4-{6-fluoro-1-methyl-9-(methoxy)-8-[(2-morpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
207	4-[8-({2-[butyl(ethyl)amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
208	4-[8-({(2R)-2-amino-3-methylbutyl}oxy)-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
209	2-chloro-4-(6-fluoro-1-methyl-9-(methoxy)-8-{{2-(1-methylpiperidin-4-yl)ethyl}oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
210	2-chloro-4-[8-{{(1-ethylpiperidin-4-yl)methyl}oxy}-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
211	5-(2-amino-1,3-thiazol-4-yl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

Table 3

Entry	Name	Structure
212	5-(5-amino-1,3,4-thiadiazol-2-yl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
213	4-[8-{{(2R)-2-amino-3,3-dimethylbutyl}oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
214	2-chloro-4-[6-fluoro-1-methyl-9-(methyloxy)-8-({2-[4-(2-methylpropyl)piperazin-1-yl]ethyl}oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
215	2-chloro-4-[8-{{2-(5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl)ethyl}oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
216	2-chloro-4-[6-fluoro-1-methyl-8-({2-[4-(1-methylethyl)piperazin-1-yl]ethyl}oxy)-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
217	4-[8-{[2-(3-amino-8-azabicyclo[3.2.1]oct-8-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
218	2-chloro-4-[8-{[2-(1-ethylpiperidin-4-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
219	2-chloro-4-[8-{[2-(diethylamino)ethyl]oxy}-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
220	2-chloro-5-{6-fluoro-1-methyl-9-(methoxy)-8-[(2-pyrrolidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
221	6,9-difluoro-5-(2-imino-3-methyl-2,3-dihydro-1,3-thiazol-5-yl)-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

Table 3

Entry	Name	Structure
222	6,9-difluoro-1-methyl-5-(1,3-thiazol-5-yl)-3H-pyrazolo[3,4-c]isoquinolin-8-ol	
223	2-chloro-4-[6-fluoro-1-methyl-8-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
224	2-chloro-4-{6-fluoro-1-methyl-9-(methoxy)-8-[(3-pyrrolidin-1-ylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
225	2-chloro-4-{6-fluoro-1-methyl-9-(methoxy)-8-[(3-piperidin-1-ylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
226	2-chloro-4-{6-fluoro-1-methyl-9-(methoxy)-8-[(3-morpholin-4-ylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
227	2-chloro-4-[8-({2-[[2-(dimethylamino)ethyl](methyl)amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methoxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
228	2-chloro-4-[8-({2-[[2-(diethylamino)ethyl](methyl)amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
229	2-chloro-4-[8-({2-[[2-(dimethylamino)ethyl](ethyl)amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
230	4-[8-[(2-{bis[3-(dimethylamino)propyl]amino}ethyl)oxy]-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
231	2-chloro-4-[6-fluoro-1-methyl-8-({2-[methyl(1-methylpyrrolidin-3-yl)amino]ethyl}oxy)-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
232	2-chloro-4-[6-fluoro-1-methyl-9-(methyloxy)-8-[(2-{(2S)-2-[(methyloxy)methyl]pyrrolidin-1-yl}ethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
233	2-chloro-4-(6-fluoro-1-methyl-9-(methyloxy)-8-([2-(4-pyrrolidin-1-yl)piperidin-1-yl)ethyl]oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
234	2-chloro-4-[8-([2-(4-cyclohexylpiperazin-1-yl)ethyl]oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
235	2-[4-(2-([5-(3-chloro-4-hydroxyphenyl)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-8-yl]oxy)ethyl)piperazin-1-yl]-N-(1-methylethyl)acetamide	
236	4-[8-([2-(1,4'-bipiperidin-1'-yl)ethyl]oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
237	2-chloro-4-[6-fluoro-1-methyl-8-([2-(4-methyl-1,4-diazepan-1-yl)ethyl]oxy)-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	

Table 3

Entry	Name	Structure
238	2-chloro-4-(6-fluoro-1-methyl-9-(methyloxy)-8-{[2-(4-pyridin-2-yl)piperazin-1-yl]ethyl}oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
239	2-chloro-4-[8-{[2-(2,6-dimethylmorpholin-4-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
240	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-thiomorpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
241	2-chloro-4-[8-{[2-(2,6-dimethylpiperidin-1-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	
242	2-chloro-4-(6-fluoro-1-methyl-9-(methyloxy)-8-{[2-(octahydroquinolin-1(2H)-yl)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	

Table 3

Entry	Name	Structure
243	4-[8-({2-[bis(1-methylethyl)amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
244	4-[8-[(2-{bis[2-(methyloxy)ethyl]amino}ethyl)oxy]-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	
245	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-piperidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
246	6,9-difluoro-1-methyl-5-(1-oxidopyridin-4-yl)-3H-pyrazolo[3,4-c]isoquinolin-8-ol	

23. (currently amended) A pharmaceutical composition comprising the compound according to any one of claims 1-22 claim 1 and a pharmaceutically acceptable carrier.

24. (currently amended) A metabolite of the compound or the pharmaceutical composition according to any one of claims 1-23 claim 1.

25. (currently amended) A method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of the compound or the pharmaceutical composition according to ~~any one of claims 1-23~~ claim 1.

26. (original) The method according to claim 25, wherein the kinase is ALK.

27. (original) The method according to claim 26, wherein modulating the *in vivo* activity of ALK comprises inhibition of ALK.

28. (currently amended) A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of the compound or the pharmaceutical composition as described in ~~any one of claims 1-23~~ claim 1.

29. (currently amended) A method of screening for modulators of ALK, the method comprising combining a compound according to ~~any one of claims 1-22~~ claim 1, and at least one candidate agent and determining the effect of the candidate agent on the ALK activity.

30. (currently amended) A method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of a composition comprising a compound according to ~~any one of claims 1-22~~ claim 1 to a cell or a plurality of cells.

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